TGAAGTCTCTTCCCAAGCAAATGGGAGCTTCTTTGGACCTTGGAGCACACAGAGGATTCTACTTTCTTTAAAACTTTGTT 80

TTCAGGCAATTTCCCTGAGAACCGTTTACTTCCAGAAGATTGGTGGAGCTTGATCTGAAGGCTGGCCATGAAATCTCAAG 160

M K S Q

GTCAACATTGGTATTCCAGTTCAGATAAAAACTGTAAAGTGAGCTTTCGTGAGAAGCTTCTGATTATTGATTCAAACCTG 240

G Q H W Y S S S D K N C K V S F R E K L L I I D S N L

GGGGTCCAAGATGTGGAGAACCTCAAGTTTCTCTGCATAGGATTGGTCCCCAACAAGAAGCTGGAGAAGTCCAGCTCAGC 320

G V Q D V E N L K F L C I G L V P N K K L E K S S S A

CTCAGATGTTTTTGAACATCTCTTGGCAGAGGATCTGCTGAGTGAGGAAGACCCTTTCTTCCTGGCAGAACTCCTCTATA 400

S D V F E H L L A E D L L S E E D P F F L A E L L Y

TCATACGGCAGAAGAAGCTGCTGCAGCACCTCAACTGTACCAAAGAGGAAGTGGAGCGACTGCTGCCCACCCGACAAAGG 480

I I R Q K K L L Q H L N C T K E E V E R L L P T R Q R

GTTTCTCTGTTTAGAAACCTGCTCTACGAACTGTCAGAAGGCATTGACTCAGAGAACTTAAAGGACATGATCTTCCTTCT 560

V S L F R N L L Y E L S E G I D S E N L K D M I F L L

GAAAGACTCGCTTCCCAAAACTGAAATGACCTCCCTAAGTTTCCTGGCATTTCTAGAGAAACAAGGTAAAATAGATGAAG 640

K D S L P K T E M T S L S F L A F L E K Q G K I D E

ATAATCTGACATGCCTGGAGGACCTCTGCAAAACAGTTGTACCTAAACTTTTGAGAAACATAGAGAAATACAAAAGAGAG 720

D N L T C L E D L C K T V V P K L L R N I E K Y K R E

AAAGCTATCCAGATAGTGACACCTCCTGTAGACAAGGAAGCCGAGTCGTATCAAGGAGAGGAAGAACTAGTTTCCCAAAC 800

K A I Q I V T P P V D K E A E S Y Q G E E E L V S Q T

Fig. 1A

AGATGTTAAGACATTCTTGGAAGCCTTACCGAGGGCAGCTGTGTACAGGATGAATCGGAACCACAGAGGCCTCTGTGTCA 880

D V K T F L E A L P R A A V Y R M N R N H R G L C V

TTGTCAACAACCACAGCTTTACCTCCCTGAAGGACAGACAAGGAACCCATAAAGATGCTGAGATCCTGAGTCATGTGTTC 960

I V N N H S F T S L K D R Q G T H K D A E I L S H V F

CAGTGGCTTGGGTTCACAGTGCATATACACAATAATGTGACGAAAGTGGAAATGGAGATGGTCCTGCAGAAGCAGAAGTG 1040

Q W L G F T V H I H N N V T K V E M E M V L Q K Q K C

CAATCCAGCCCATGCCGACGGGGACTGCTTCGTGTTCTGTATTCTGACCCATGGGAGATTTGGAGCTGTCTACTCTTCGG 1120

N P A H A D G D C F V F C I L T H G R F G A V Y S S

ATGAGGCCCTCATTCCCATTCGGGAGATCATGTCTCACTTCACAGCCCTGCAGTGCCCTAGACTGGCTGAAAAACCTAAA 1200

D E A L I P I R E I M S H F T A L Q C P R L A E K P K

CTCTTTTTCATCCAGGCCTGCCAAGGTGAAGAGATACAGCCTTCCGTATCCATCGAAGCAGATGCTCTGAACCCTGAGCA 1280

L F F I Q A C Q G E E I Q P S V S I E A D A L N P E Q

GGCACCCACTTCCCTGCAGGACAGTATTCCTGCCGAGGCTGACTTCCTACTTGGTCTGGCCACTGTCCCAGGCTATGTAT 1360

A P T S L Q D S I P A E A D F L L G L A T V P G Y V

CCTTTCGGCATGTGGAGGAAGGCAGCTGGTATATTCAGTCTCTGTGTAATCATCTGAAGAAATTGGTCCCAAGACATGAA 1440

S F R H V E E G S W Y I Q S L C N H L K K L V P R H E

GACATCTTATCCATCCTCACTGCTGTCAACGATGATGTGAGTCGAAGAGTGGACAAACAGGGAACAAAGAAACAGATGCC 1520

D I L S I L T A V N D D V S R R V D K Q G T K K Q M P

CCAGCCTGCTTTCACACTAAGGAAAAAACTAGTATTCCCTGTGCCCCTGGATGCACTTTCAATATAGCAGAGAGTTTTTG 1600

Q P A F T L R K K L V F P V P L D A L S I

NTGGTTCTTAGACCTCAAACGAATCATTGGGNTATAACCTCCAGCCTCCTGCCCAGCACAGGAATCGGTGGTCTCCACCTG 1680

TCATTCTAGAAACAGGAAAC 1700

Fig. 1B

TGAAGGCTGGTTGTTCAGACTGAGCTTTCCTGCCTGCCTGTACCCCGCCAACAGCTTCAGAAGAAGGTGACTGGTGGCTGC 80

CTGAGGAATACCAGTGGGCAAGAGAATTAGCATTTCTGGAGCATCTGCTGTCTGAGCAGCCCCTGGGTGCGTCCACTTTC 160

TGGGCACGTGAGGTTGGGCCTTGGCCGCCTGAGCCCTTGAGTTGGTCACTTGAACCTTGGGAAATATTGAGATTATATTCT 240

CCTGCCTTTTAAAAAGATGGACTTCAGCAGAAATCTTTATGATATTGGGGAACAACTGGACAGTGAAGATCTGGCCTCCC 320

M D F S R N L Y D I G E Q L D S E D L A S

TCAAGTTCCTGAGCCTGGACTACATTCCGCAAAGGAAGCAAGAACCCATCAAGGATGCCTTGATGTTATTCCAGAGACTC 400

L K F L S L D Y I P Q R K Q E P I K D A L M L F Q R L

CAGGAAAAGAGAATGTTGGAGGAAAGCAATCTGTCCTTCCTGAAGGAGCTGCTCTTCCGAATTAATAGACTGGATTTGCT 480

Q E K R M L E E S N L S F L K E L L F R I N R L D L L

GATTACCTACCTAAACACTAGAAAGGAGGAGATGGAAAGGGAACTTCAGACACCAGGCAGGGCTCAAATTTCTGCCTACA 560

I T Y L N T R K E E M E R E L Q T P G R A Q I S A Y

GGTTCCACTTCTGCCGCATGAGCTGGGCTGAAGCAAACAGCCAGTGCCAGACACAGTCTGTACCTTTCTGGCGGAGGGTC 640

R F H F C R M S W A E A N S Q C Q T Q S V P F W R R V

GATCATCTATTAATAAGGGTCATGCTCTATCAGATTTCAGAAGAAGTGAGCAGATCAGAATTGAGGTCTTTTAAGTTTCT 720

D H L L I R V M L Y Q I S E E V S R S E L R S F K F L

TTTGCAAGAGGAAATCTCCAAATGCAAACTGGATGATGACATGAACCTGCTGGATATTTTCATAGAGATGGAGAAGAGGG 800

L Q E E I S K C K L D D D M N L L D I F I E M E K R

TCATCCTGGGAGAAGGAAAGTTGGACATCCTGAAAAGAGTCTGTGCCCAAATCAACAAGAGCCTGCTGAAGATAATCAAC 880

V I L G E G K L D I L K R V C A Q I N K S L L K I I N

GACTATGAAGAATTCAGCAAAGGGGAGGAGTTGTGTGGGGTAATGACGATGTCGGACTGTCCAAGAGAACAGGATAGTGA 960

D Y E E F S K G E E L C G V M T M S D C P R E Q D S E

Fig. 2A

ATCACAGACTTTGGACAAAGTTTACCAAATGAAAAGCAAGCCTCGGGGATACTGTCTGATCATCAACAATCACAATTTTG 1040

S Q T L D K V Y Q M K S K P R G Y C L I I N N H N F

CAAAAGCACGGGAGAAAGTGCCCAAACTTCACAGCATTAGGGACAGGAATGGAACACACTTGGATGCAGGGGCTTTGACC 1120

A K A R E K V P K L H S I R D R N G T H L D A G A L T

ACGACCTTTGAAGAGCTTCATTTTGAGATCAAGCCCCACCATGACTGCACAGTAGAGCAAATCTATGAGATTTTGAAAAT 1200

T T F E E L H F E I K P H H D C T V E Q I Y E I L K I

CTACCAACTCATGGACCACAGTAACATGGACTGCTTCATCTGCTGTATCCTCTCCCATGGAGACAAGGGCATCATCTATG 1280

Y Q L M D H S N M D C F I C C I L S H G D K G I I Y

GCACTGATGGACAGGAGGCCCCCATCTATGAGCTGACATCTCAGTTCACTGGTTTGAAGTGCCCTTCCCTTGCTGGAAAA 1360

G T D G Q E A P I Y E L T S Q F T G L K C P S L A G K

CCCAAAGTGTTTTTTATTCAGGCTTGTCAGGGGGATAACTACCAGAAAGGTATACCTGTTGAGACTGATTCAGAGGAGCA 1440

P K V F F I Q A C Q G D N Y Q K G I P V E T D S E E Q

ACCCTATTTAGAAATGGATTTATCATCACCTCAAACGAGATATATCCCGGATGAGGCTGACTTTCTGCTGGGGATGGCCA 1520

P Y L E M D L S S P Q T R Y I P D E A D F L L G M A

CTGTGAATAACTGTGTTTCCTACCGAAACCCTGCAGAGGGAACCTGGTACATCCAGTCACTTTGCCAGAGCCTGAGAGAG 1600

T V N N C V S Y R N P A E G T W Y I Q S L C Q S L R E

CGATGTCCTCGAGGCGATGATATTCTCACCATCCTGACTGAAGTGAACTATGAAGTAAGCAACAAGGATGACAAGAAAAA 1680

R C P R G D D I L T I L T E V N Y E V S N K D D K K N

CATGGGGAAACAGATGCCTCAGCCTACTTTCACACTAAGAAAAAAACTTGTCTTCCCTTCTGATTGATGGTGCTATTTTG 1760

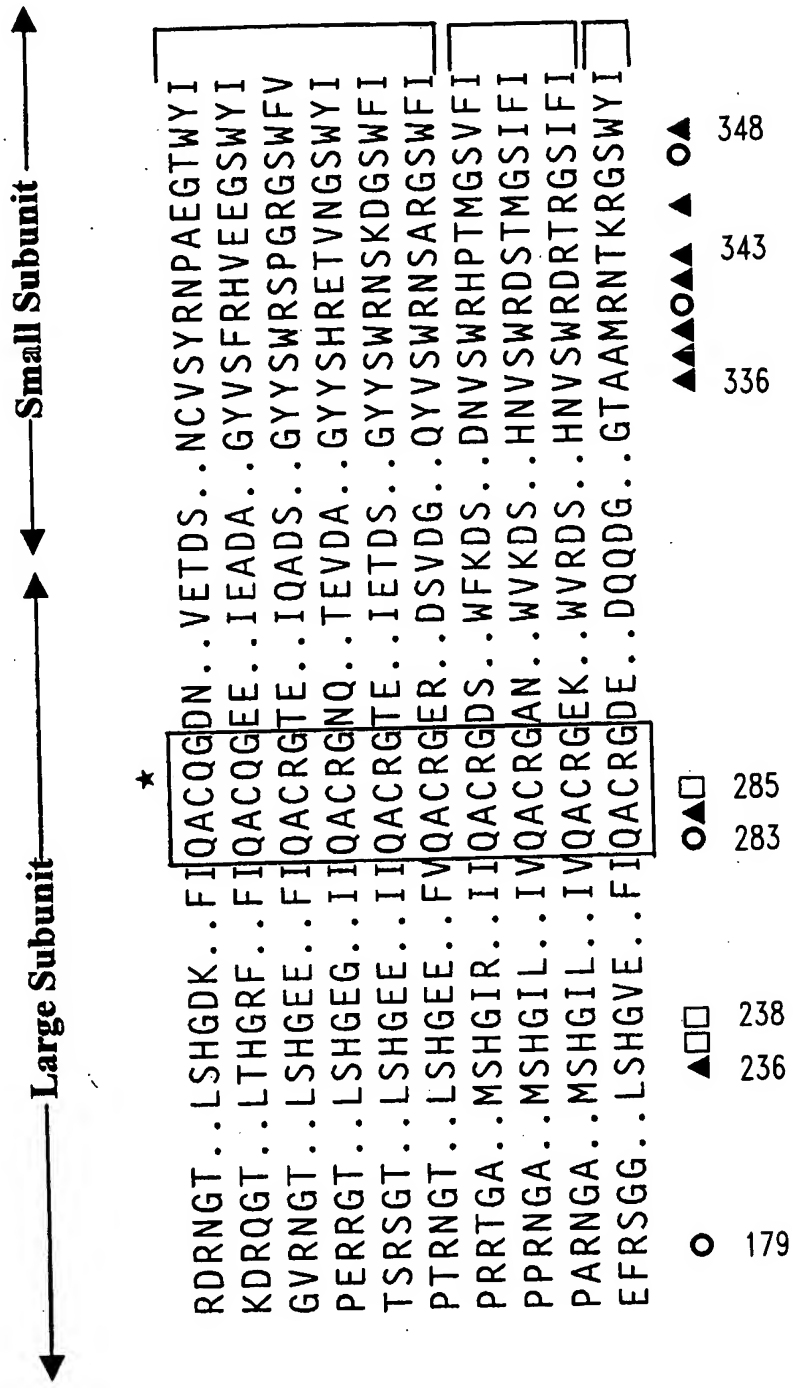
M G K Q M P Q P T F T L R K K L V F P S D

TTTGTTTTGTTTTGTTTTGTTTTTTTGAGACAGAATCTCGCTCTGTCGCCCAGGCTGGAGTGCAGTGGCGTGATCTCGGC 1840

TCACCGCAAGCTCCGCCTCCCGGGTTCAGGCCATTCTCCTGCT 1883

Fig. 2B

Fig. 3A


Large Subunit
Small Subunit
I
II
III
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Mch3 GVRNGT..LSHGEE..FIQACRGTE..IQADS..GYYSWRSPGRGSWFV
Mch2 PERRGT..LSHGEG..IIQACRGNQ..TEVDA..GYYSHRETVNGSWYI
CPP32 TSRSGT..LSHGEE..IIQACRGTE..IETDS..GYYSWRNSKDGSWFI
CED-3 PTRNGT..LSHGEE..FVQACRGER..DSVDG..QYVSWRNSARGSWFI
ICE PRRTGA..MSHGIR..IIQACRGDS..WFKDS..DNVSWRHPTMGSVFI
TX PPRNGA..MSHGIL..IVQACRGAN..WVKDS..HNVSWRDSTMGSIFI
ICErel PARNGA..MSHGIL..IVQACRGEK..WVRDS..HNVSWRDRTRGSIFI
ICH-1 EFRSGG..LSHGVE..FIQACRGDE..DQQDG..GTAAMRNTKRGSWYI
179
236
238
283
285
336
343
348

Fig. 3B

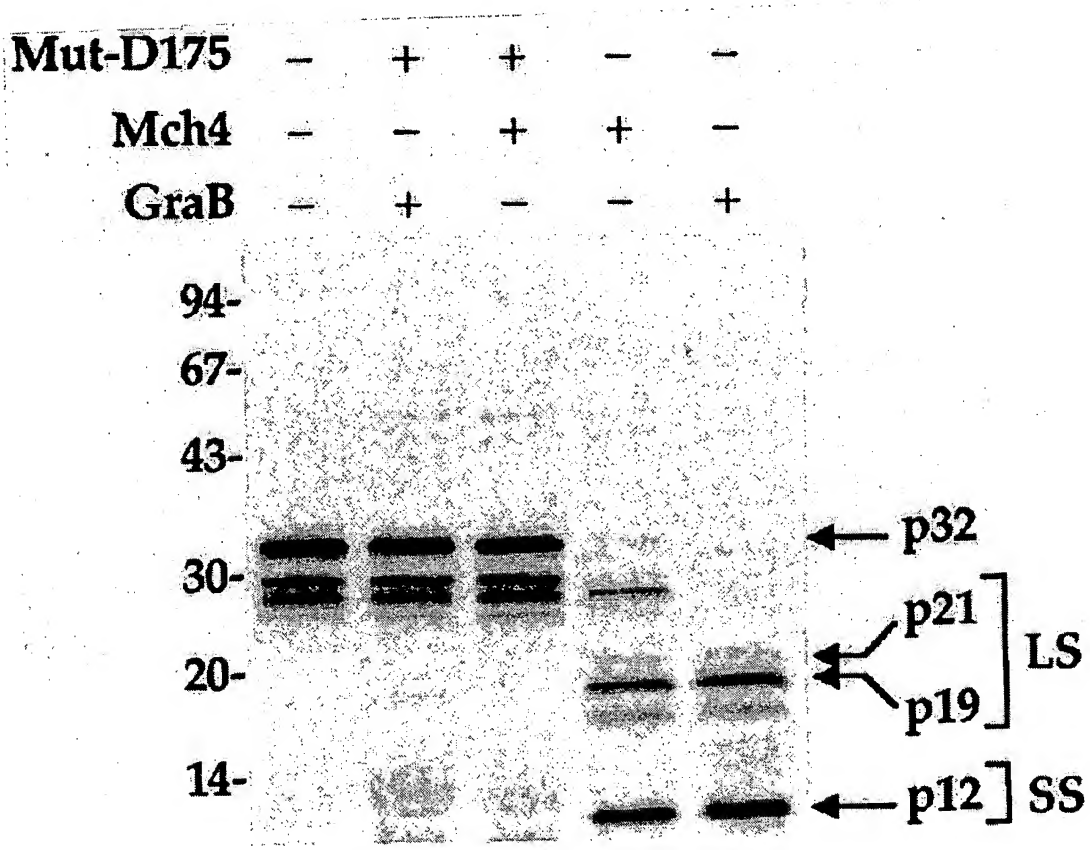

Fig. 4A

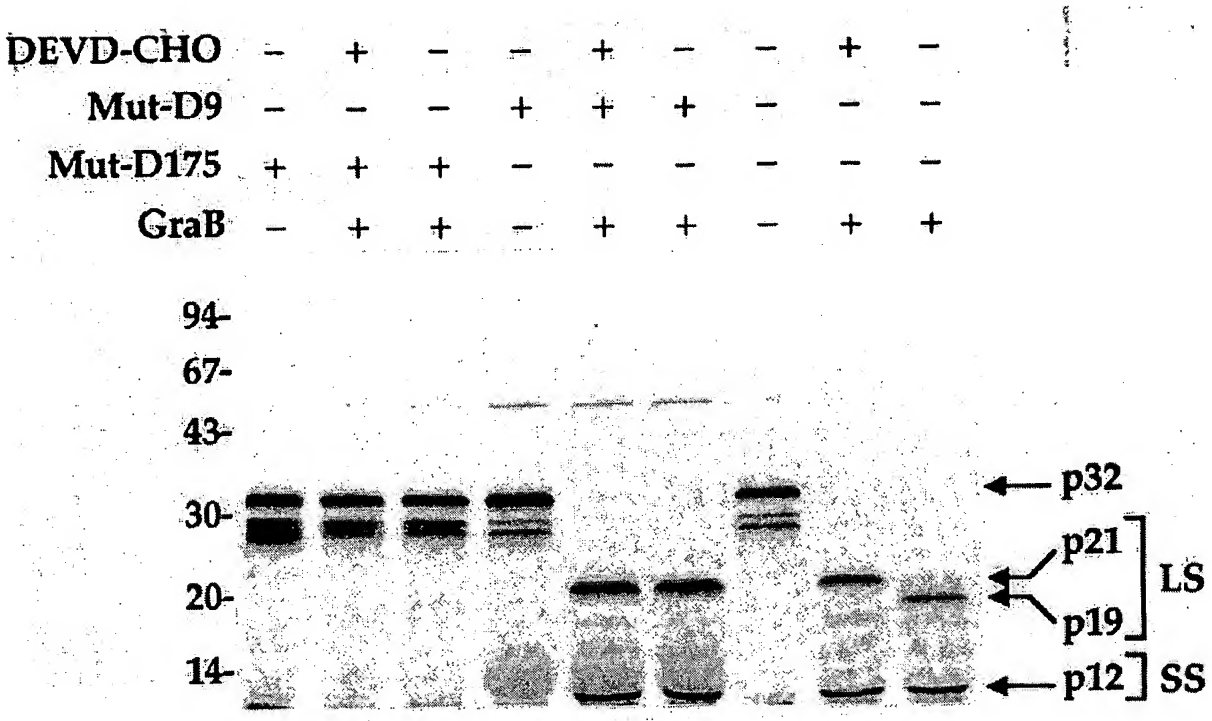
DEVD-CHO – + – – + – – + –
Mut-D9 – – – + + + – – –
Mut-D175 + + + – – – – – –
GraB – + + – + + – + +
94-
67-
43-
30-
20-
14-
p32
p21
p19
LS
p12
SS

Fig. 4B

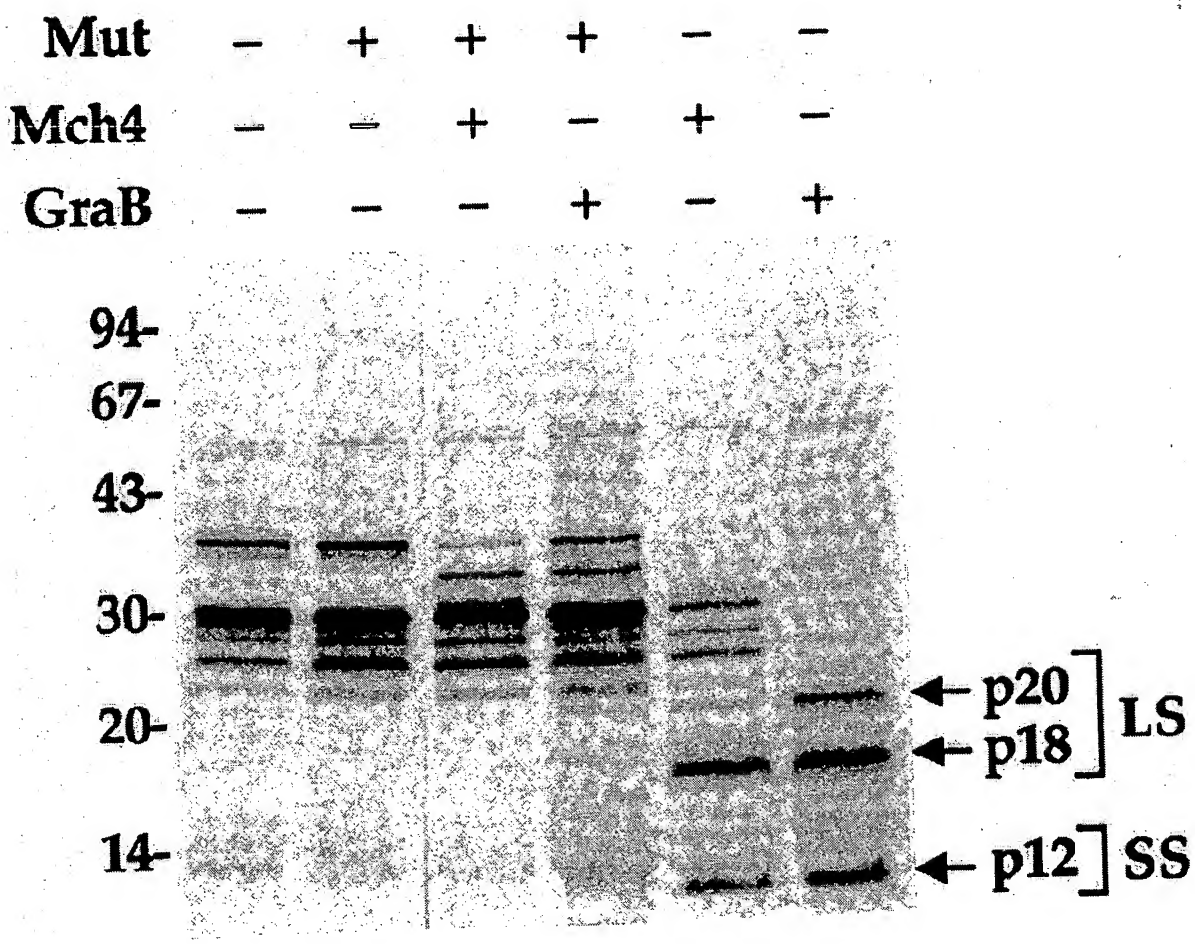

Fig. 5A

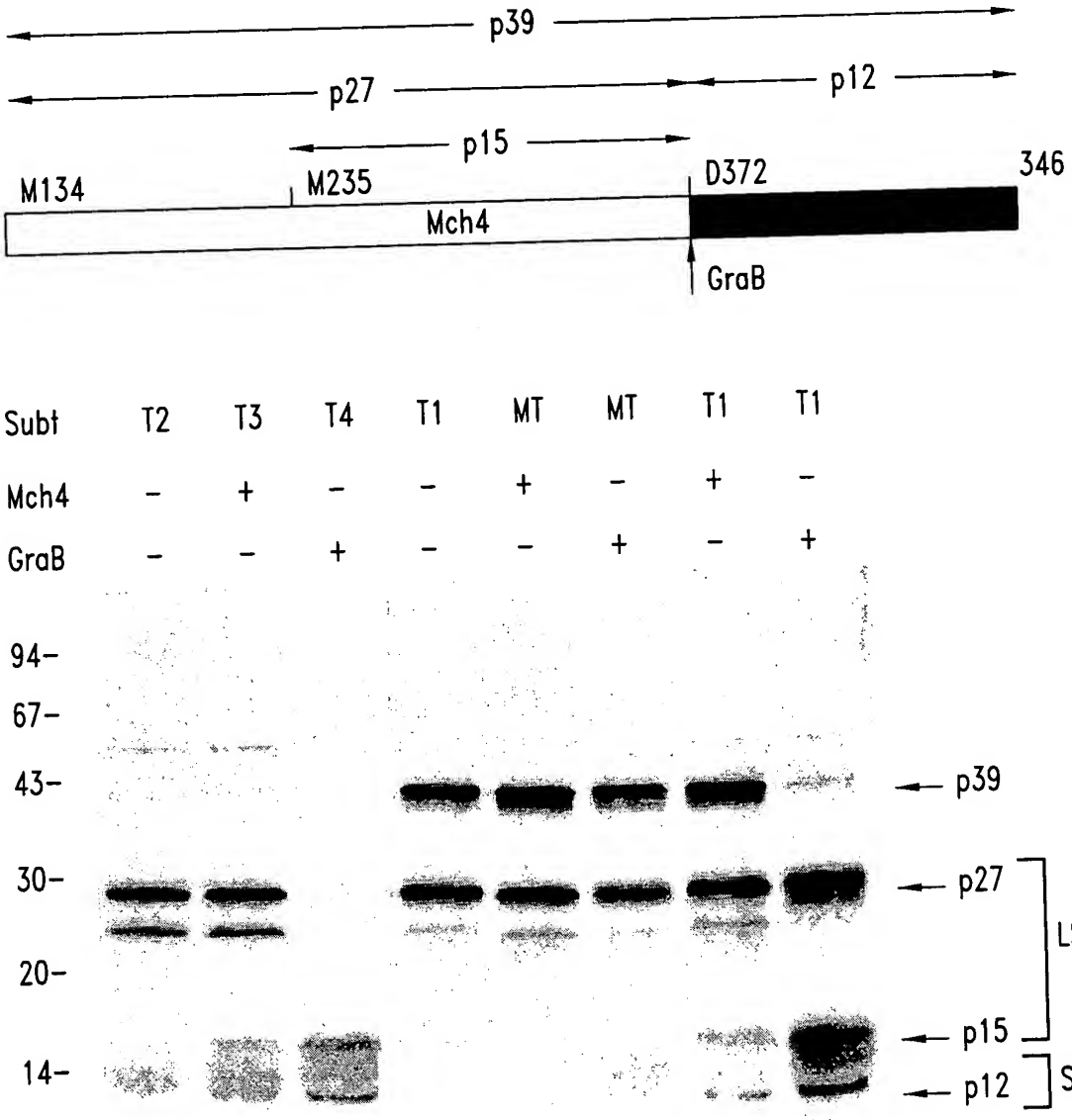
p39
p27
p12
p15
M134
M235
D372
346
Mch4
GraB
Subt
T2
T3
T4
T1
MT
MT
T1
T1
Mch4
GraB
94-
67-
43-
30-
20-
14-
p39
p27
p15
p12
LS
SS

Fig. 5B

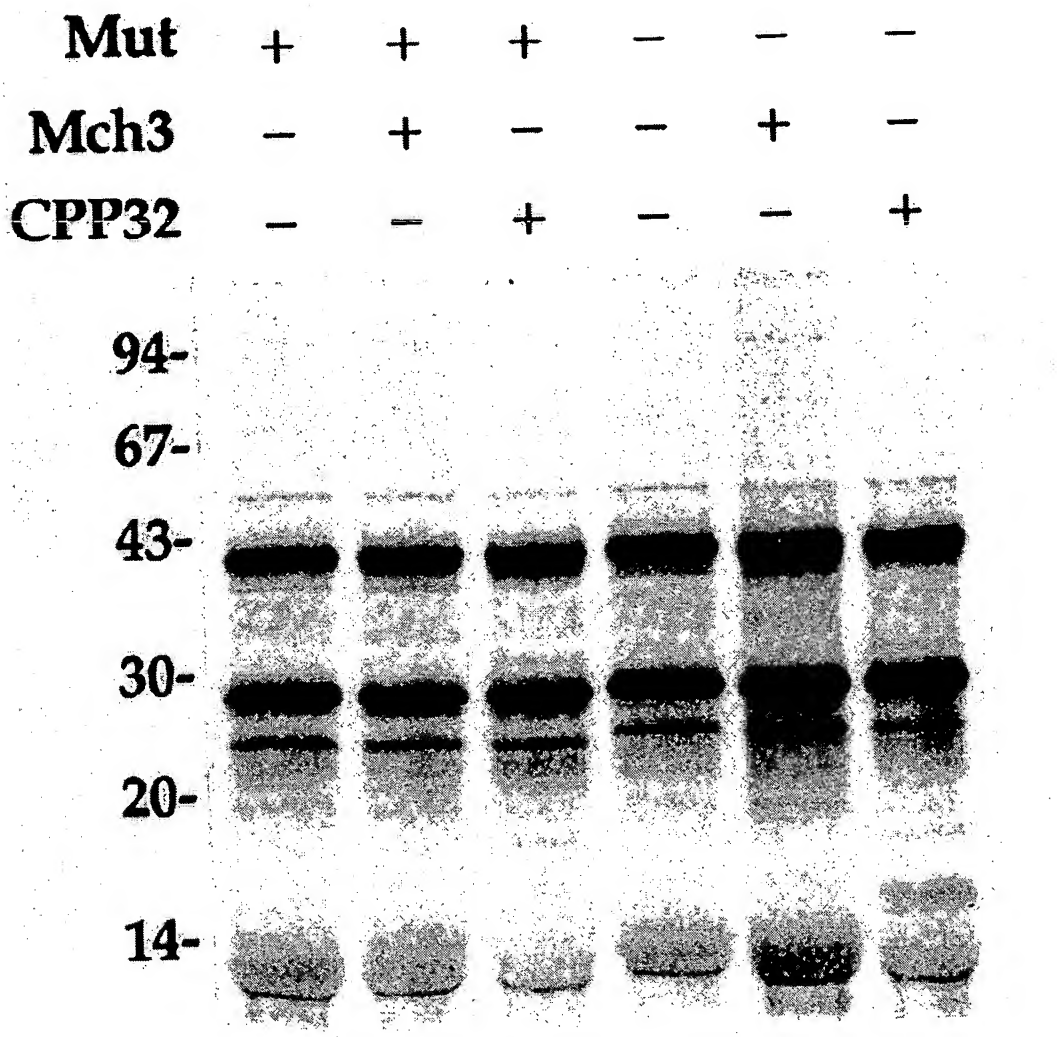

Fig. 6

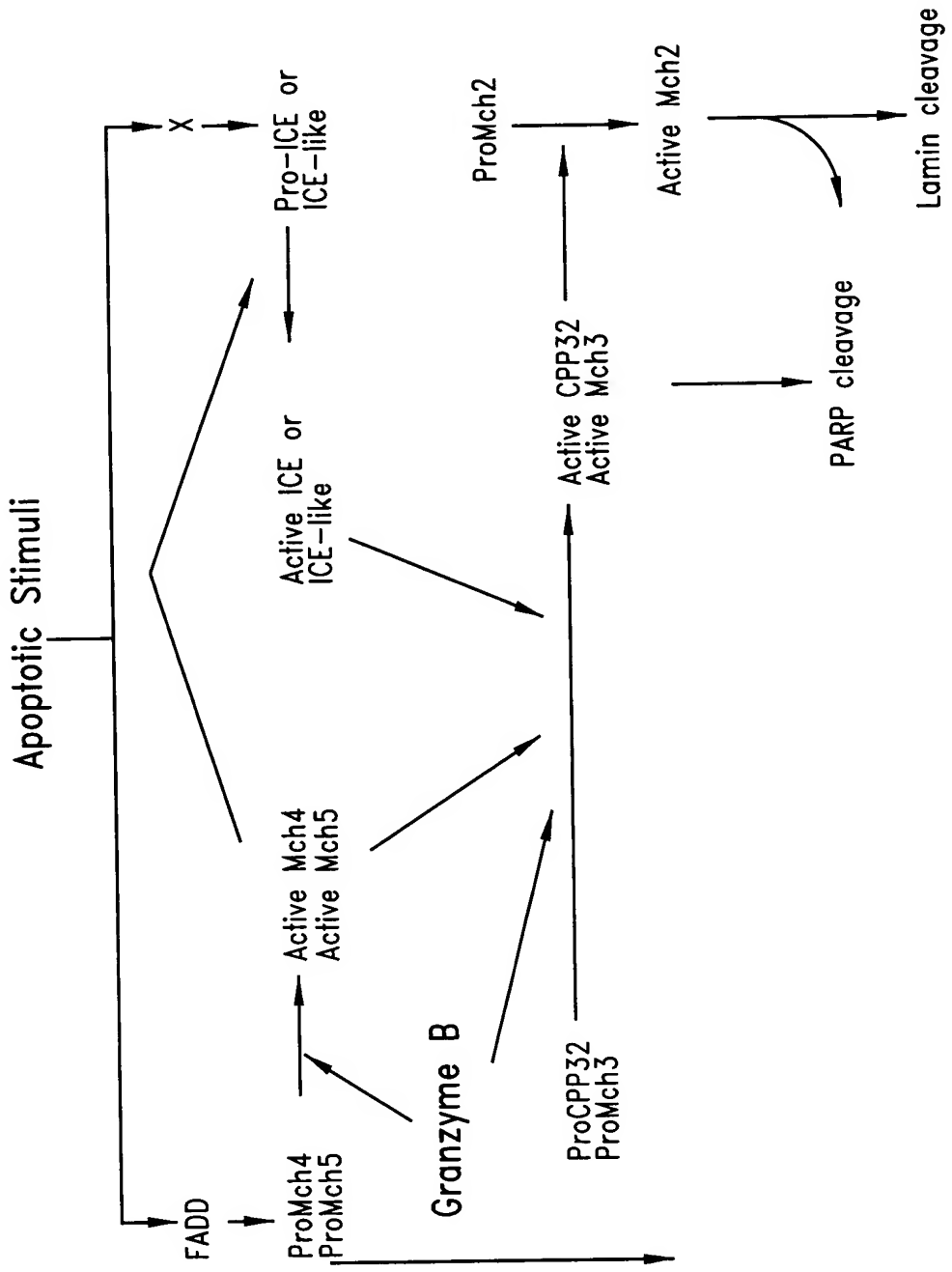
Apoptotic Stimuli
X
Pro-ICE or
ICE-like
Active ICE or
ICE-like
ProMch2
Active Mch2
Lamin cleavage
PARP cleavage
Active CPP32
Active Mch3
Active Mch4
Active Mch5
Granzyme B
ProCPP32
ProMch3
FADD
ProMch4
ProMch5
Apoptotic phenotype

Fig. 7

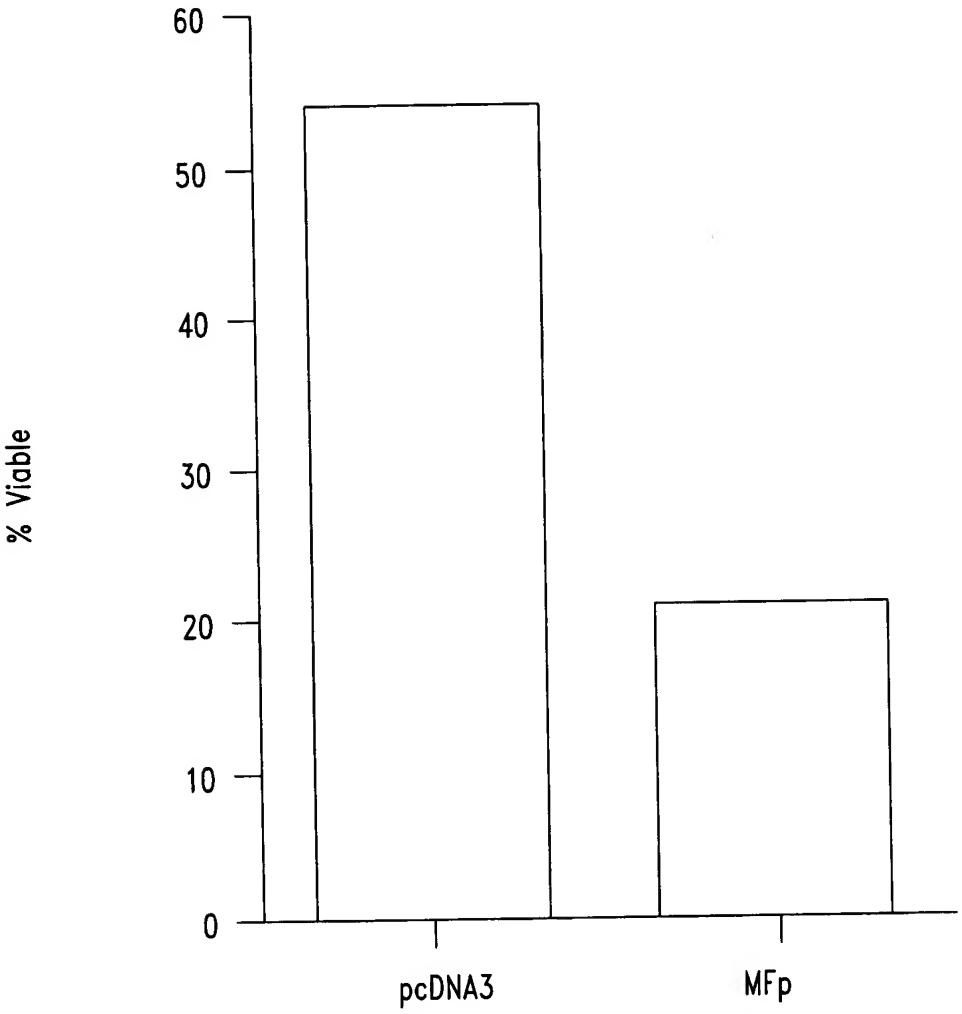

Fig. 8